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REVIEWS

Participation of Septin Cytoskeletal Proteins in the Nervous System Functioning

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Abstract—Septins, the cytoskeletal proteins discovered in the 1970s in budding yeast cells, are currently detected in most postmitotic cells of animals and humans. In the last decade, significant progress has been made in understanding the biochemical properties of septins and their biological functions. An increasing number of studies show that these proteins play an important role in the development and physiology of specific tissues and organs. The review surveys classification, major functions and localization of septins in the nervous system of mammals and humans. Models describing the mechanisms of the septin involvement in the neurotransmitter secretion from nerve endings and the role of septins in the pathogenesis of various neurodegenerative diseases are discussed.

Keywords: cytoskeletal proteins, nervous system, septins, neurotransmitter secretion

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INTRODUCTION

Septins are a conservative family of GTP-binding proteins. They were first identified in dividing *Saccharomyces cerevisiae* yeast cells [1]. Over the past four decades, septins were found in various eukaryotic cells of mammals and humans [2, 3]. Significant progress has been made in understanding the biochemical properties and biological functions of septins [4, 5]. An increasing number of studies show that septins play an important role in the development and physiology of various tissues and organs [6, 7]. Septins are denoted as SEPT1–SEPT14, depending on the encoding gene number. The genes of 14 septin subtypes were detected in the human genome, which were conventionally divided into four groups, based on similarities of the amino acid sequences [7, 8]:

Group I, SEPT2; includes SEPT1, SEPT2, SEPT4, SEPT5;

Group II, SEPT3; includes SEPT3, SEPT9, and SEPT12;

Group III, SEPT6; includes SEPT6, SEPT8, SEPT10, SEPT11, and SEPT14;

Group IV, SEPT7; includes SEPT7, SEPT13.

More than 30 septin isoforms which differ in their functions are formed as a result of alternative splicing [8]. Table 1 presents the main septin subtypes, their localization in the central nervous system, functions, and neurological disorders when septin expression changes are observed.

STRUCTURE AND MAIN FUNCTIONS OF SEPTINS

Septins consist of basic amino acid residues and GTP-binding domains. A typical septin structure is shown in Fig. 1a. The nucleotide-binding domain of these proteins consists of alternating α-helices and β-strands separated by flexible loops containing motifs interacting with the phosphate groups of GTP or ATP. This domain determines the specificity of protein binding, and its amino acid sequence differs in different septin subgroups. The N-terminus of septins associates with phosphoinositides of plasma and vesicular membranes [4, 9]. The C-terminus of these proteins is conservative and is required for interaction with other septins and formation of septin complexes [4, 9, 13]. Septins differ mainly in the length and amino acid composition of the N- and C-termini, which contain regions enriched in proline residues and α-helical loops. In 2007, Sirajuddin et al. [14] established for the first time the crystal structure of the SEPT2/SEPT6/SEPT7 complex, the most common in mammals, including humans (Fig. 1b) [8]. The ability of this complex to form highly organized structures with mirror symmetry with the order SEPT7–SEPT6–SEPT2–SEPT2–SEPT6–SEPT7 was shown.

The basic biological septin functions are associated with their ability to form dimers and combine into filamentous polymers, which can form rings, spirals and nets, and serve as cell scaffolds, so-called scaffold proteins (Fig. 1c). Septin complexes serve as diffusion